

# A unique case of pregnancy-induced parathyroid hyperplasia with severe hypercalcemia

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## CASE REPORT

30-year-old woman G1P0 at 24 weeks of gestation

### History of Present Illness

- New onset **nausea/vomiting, headache** x 2 weeks
- BP **160/100**; HR 90; SaO<sub>2</sub> 100%; Afebrile
- Thyroid/Heart/Lungs/Abdomen/Neuro normal
- No edema

### Family History

No hypercalcemia/MEN. 1 sister with no pregnancy complications.

### INVESTIGATIONS

LABORATORY TEST	VALUE	REFERENCE	RANGE
Creatinine	<b>154 Umol/L</b>	↑	46-92
Na	133 mmol/L	↓	135-145
K	3.7 mmol/L	N	3.5-5.1
Total adjusted Calcium	<b>4.79 mmol/L</b>	↑	2.07-2.55
Ionized Calcium	<b>2.33 mmol/L</b>	↑	1.12-1.32
Albumine	34.4 g/L	↓	35-52
PTH	<b>31 pmol/L</b>	↑	1.6-6.9
PTHrp	13 ng/L	N	1.0-15.0
25-OH-D	62 nmol/L	↓	75-150
Phosphate	0.62 mmol/L	↓	0.87-1.45
Magnesium	0.69 mmol/L	↓	0.75-1.00

### Imaging

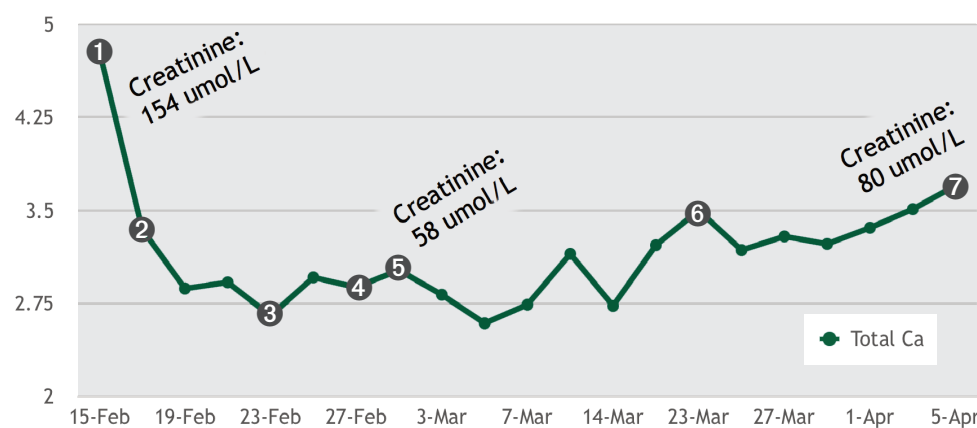
- **Neck Ultrasound (US):** Normal
- **Neck MRI:** 2 hyperintense nodules behind the right thyroid lobe and below the right mainstem bronchus
- **CT-4D:** 2 hypervascular micronodules compatible with parathyroid glands
- **Renal US:** Mild bilateral hydronephrosis. Mild medullary nephrocalcinosis.

### Fetal evaluation

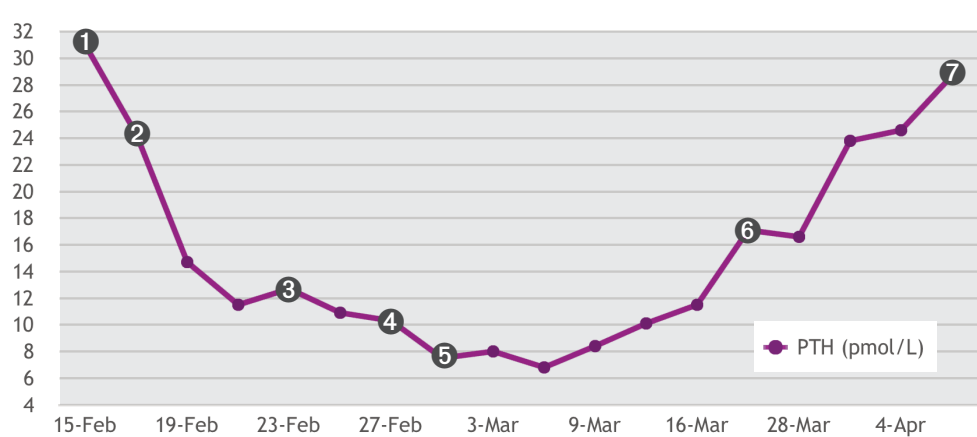
Normal fetal growth, amniotic fluid and well-being

## ANTEPARTUM MANAGEMENT

### TOTAL CALCIUM ANTEPARTUM (mmol/L)



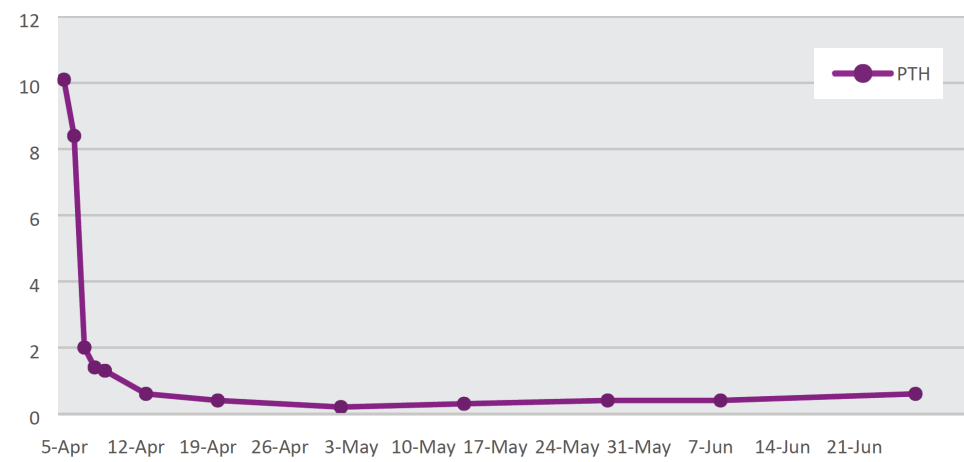
### PTH ANTEPARTUM (pmol/L)



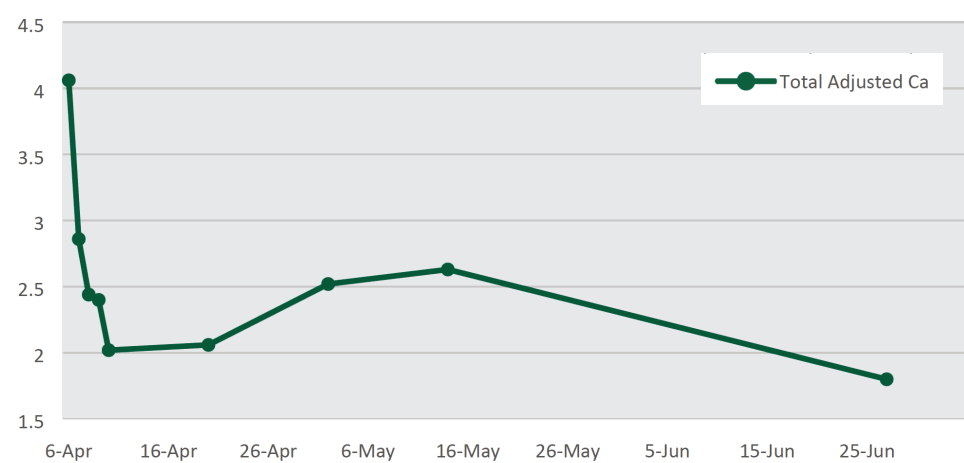
1. IV Hydration; Adalat XL 30 mg BID  
**Calcitonin 4UI/kg s/c q 12h:** Does not cross the placenta
2. **Surgery #1:** Parathyroidectomy of 2 1/2 glands, 1/2 left in place, 4<sup>th</sup> gland not found. Pathology: Glandular Hyperplasia
3. Parathyroid Scintigraphy: No parathyroid or ectopic adenoma
4. **Surgery #2:** The 1/2 gland left was removed and implanted in the arm. **Surgery #3:** Neck exploration and right hemithyroidectomy + Mediastinoscopy; 4<sup>th</sup> gland not found
5. **Cinacalcet 30 mg po BID:** N=6 pregnancies, 1 case with neonatal hypocalcemia, no bone defects at 2 y.o
6. Hydration IV + Lasix IV. **Surgery #4:** removal of the 1/2 gland in the arm. **Bisphosphonates?** Cross placenta. Skeletal defects in animals, 160 cases of fetal exposure: Hypocalcemia, no bone defects. Our decision: NOT to use since uncertain benefit and potential harm
7. **Caesarean section** at 31 weeks of gestation

## POST-PARTUM COURSE

### PTH POST-PARTUM (pmol/L)



### TOTAL CALCIUM POST-PARTUM (mmol/L)



### Follow-up post-partum

#### BABY

- Born with Total adjusted Calcium 3.54 mmol/L & Ionized Calcium 1.87 mmol/L; PTH 0.4 pmol/L. Normalized after 8 hours of life.
- No hypocalcemia or complication
- Discharge from neonatal care at 53 days of life without major complication
- Now 5 months old with normal development

#### MOTHER

- Symptomatic hypocalcemia at PO#6: Total adjusted Calcium 2.03 mmol/L; PTH 0.4 pmol/L
- Treatment: Calcitriol 0.5 mg po TID + Calcium gluconate 1g po QID

### Treatment at 5 months post-partum

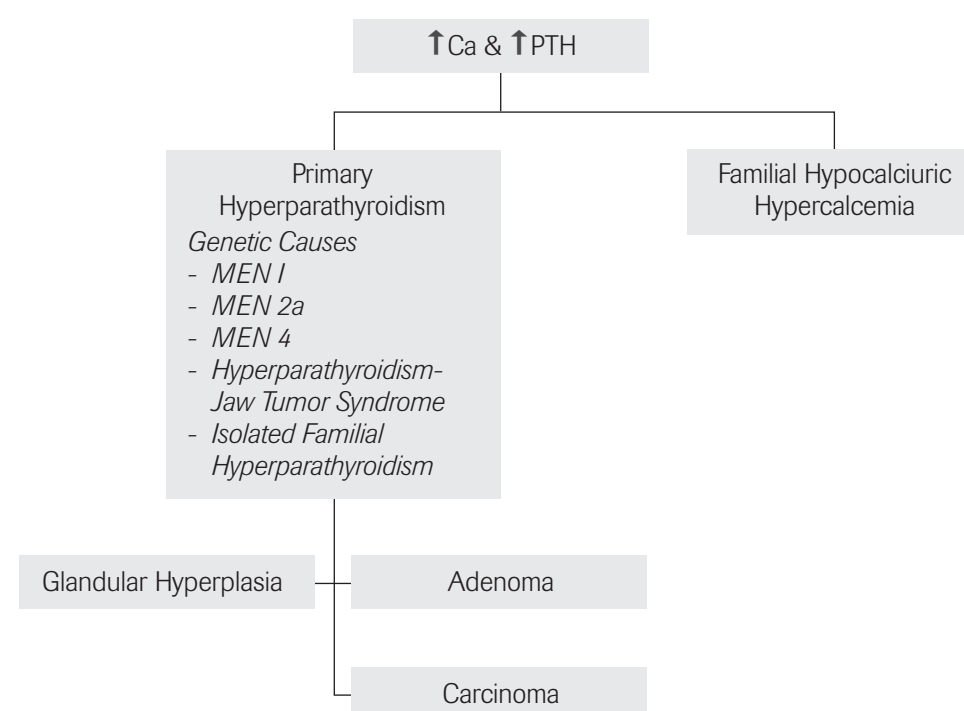
- Calcium 500 mg DIE
- Calcitriol 0.25 mg DIE
- Synthroid 0.1 mg DIE
- Mg 500 mg DIE
- Vit D 10 000 U/week

## DISCUSSION

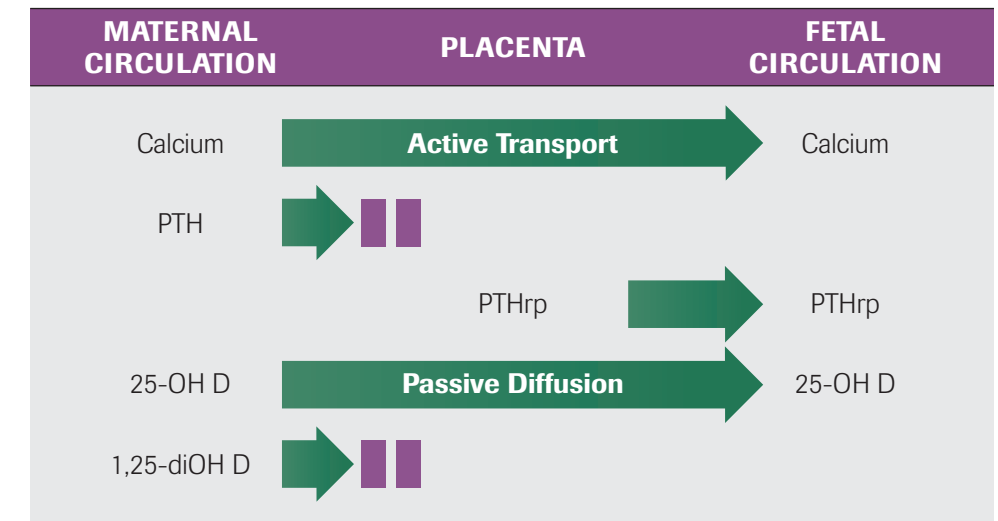
### NORMAL CALCIUM HOMEOSTASIS OF PREGNANCY

Total Calcium	↓
Ionized Calcium	Normal
Urinary Calcium	↑
PTH <sub>i</sub>	Normal or ↓
PTHrP	↑ (ad 3 x N)
25-OH D	Normal
1,25-OH <sub>2</sub> D	↑ (ad x 2 N)

### DIFFERENTIAL DIAGNOSIS



## MATERNAL-FETAL REGULATION OF CALCIUM DURING GESTATION



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## POTENTIAL EFFECTS OF HYPERCALCEMIA IN PREGNANCY

MATERNAL	FETAL
- Hyperemesis gravidarum	- Neonatal hypoparathyroidism
- Preeclampsia/Hypertension	- Hypocalcemia/Tetany
- Nephrolithiasis	- Mental retardation
- Osteoporosis	- Low birth weight
- Pancreatitis	- <b>Stillbirth:</b>
- Psychiatric	- Pregnancy outcomes are similar to general population in large cohort studies and case series, but intrauterine fetal death have been reported
	- Majority of cases have mild to moderate hypercalcemia with highest calcium reported at 3.64 mmol/L
	- Literature suggests that treatment/surgery is not mandatory if Ca < 2.75 mmol/L
	- Difficult to estimate stillbirth risk with such high calcium in our case

### Hypothesis

- First case of pregnancy-induced hyperparathyroidism from rapidly reversible pregnancy-induced PTH hypersecretion and parathyroid hyperplasia
- Analogy with a case of a Cushing syndrome induced by pregnancy where hCG stimulated receptors on adrenal glands. Cushing syndrome was recurrent at each pregnancy.
- Implications for the next pregnancy: unknown but potentially high likelihood of recurrence

### Perspective

- Genetic screening for MEN and parathyroid hyperplasia and full exome sequencing under way

## CONCLUSION

- Consider hypercalcemia in a pregnant patient with new onset of nausea/vomiting in T2-T3 and hypertension
- The safe level of serum calcium in pregnancy is unknown
- Treatment is challenging since little is known about cinacalcet and bisphosphonates in pregnancy
- Multidisciplinary team was an essential key to the meticulous step by step management of that difficult case

### REFERENCES

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